Central Nervous System

Ass. Prof. Wessam Ezzat

Consciousness &

- **Consciousness:** It is the awareness of self & one's surroundings, thoughts and feelings.
- Consciousness (wakefulness) is produced by general excitation of the cerebral cortex as a result of activation of ARAS and is maintained by positive feedback mechanism between cortex and ARAS.
- **Sleep:** It is a state of temporary unconsciousness from which person can be aroused by sensory or motor stimuli.

▪ Physiology (mechanism) of consciousness (wakefulness):

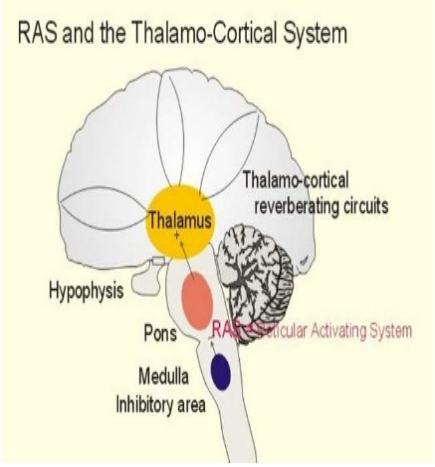
- The initiation and maintenance or consciousness is the function of the ascending reticular activating system (= ARAS). Activation of this system leads to consciousness (through excitation of the cerebral cortex by signals discharged via the *reticulo-thalamo-cortical* pathway).
- Consciousness is then maintained by a *+ve feedback mechanism* through re-excitation of the RAS by signals discharged from the activated cortex via the *corticofugal.fibres* (which constitute a *cortico-thalamo-reticular pathway).*

Note: The ascending reticular activating system (ARAS or RAS)

It is a complex multineuronal polysynaptic pathway of nerve fibers that originate at the facilitatory reticular formation. The majority of fibers extends upwards to the non specific thalamic nuclei (intralaminar and reticular nuclei of thalamus), from which other fibers arises and project diffusely to almost all parts of cerebral cortex. This pathway is called ***reticulo-thalamo-cortical pathway***.

Function of ARAS:

It controls the electrical activity the cerebral cortex and is concerned with consciousness and production of alert



The ascending reticular

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▪ Physiological changes during sleep:

1- Circulatory system : The heart rate, vasomotor tone and arterial blood pressure are all decreased.

2- Respiratory system: The rate and depth of respiration are decreased *(so pulmonary ventilation is decreased with a tendency to acidosis).*

3- Nervous system: Most reflexes disappear, the voluntary activity and sensory perception are abolished and *a positive Babinski's sign* is obtained.

4- The skeletal muscle tone, body temperature and metabolic rate are all decreased.

5- Most endocrine secretions are decreased (but secretion of the growth hormone increases during sleep). On the other hand the secretions of the GIT tend to increase during sleep.

▪ Importance of sleep:

1- Provides the brain with time to restore biochemical or physiological processes that have progressively decreased during wakefulness.

2- Sleep is important for consolidation of memory & for learning

▪ Neurochemical mechanisms (theories) of sleep:

- Transitions between sleep and wakefulness manifest a circadian rhythm consisting of an average of 8 h of sleep and 16 h of wakefulness. Nuclei in both the brain stem and hypothalamus are critical for the transitions between these states of consciousness.
- Sleep is primarily results from depression or the cerebral cortex *secondary to inhibition of the ARAS activity.* ARAS inhibition can occur by either:

1- Passive theory of sleep:

Sleep is caused by passive inhibition of ARAS by fatigue after a period of wakefulness or by decreasing its activity through elimination of exciting stimuli e.g visual, auditory, painful and other stimuli.

2- Active theory of sleep:

- The brainstem RAS is composed of several groups of neurons which release *norepinephrine* (from locus cerulus), *serotonin* (raphe nucleus). Also forebrain neurons are involved in control of the sleep–wake cycles e.g preoptic neurons in the *anterior* hypothalamus release GABA and *posterior* hypothalamic neurons release histamine.

- Many area with NT are involved in production of wakefulness state as
  - Noradrenaline from locus cerulus.
  - Serotonin from raphe nucleus.
  - Orexins from hypothalmus (lateral hypothalamic area=LHA).
  - Histamine from post. hypothalamus (tuberomammillary nuclei=TMN).

- Sleep is caused by active inhibition of ARAS through stimulation of specific areas of the brain. For example, the ventrolateral preoptic area in the posterior hypothalamus secretes an inhibitory neurotransmitter named GABA which inhibits many brain stem nuclei which are part of the RAS such as the raphe nucleus (serotonin), locus cerulus (norepinephrine) and posterior hypothalamus (histamine) resulting in sleep.

- One explanation regarding the basis of transition from sleep to wakefulness involves alternating reciprocal activity of different groups of RAS neurons. When the activity of norepinephrine and serotonin containing neurons (locus ceruleus and raphe nuclei) is dominant, this pattern of activity contributes to the appearance of the wakefulness state. The reverse of this pattern (when the activity of norepinephrine and serotonin containing neurons is less) lead to REM sleep.

▪ Types of sleep:

There are 2 types of sleep that normally *alternate with each other:*

1- Slow wave sleep = non-rapid eye movement or non-REM sleep:

- This type is the first to occur when the person falls asleep. It is characterized by *slow EEG waves and absence of REM.*
- It occupies most of the sleeping duration (80%) of total sleeping hours in adults and it is longer early in night.

✓ **EEG changes:**

EEG recordings during this type of sleep pass in 4 stages that occur respectively as follows:

- ***Stage 1:*** Sleep is very light (theta waves) (4-7 Hz)
- ***Stage 2:*** Sleep is light (sleep spindles (bursts of large alpha waves 12-15 Hz) and K complexes (large and slow potential) are seen within theta waves).

- ***Stage 3:*** Sleep is moderate (delta waves (3-3.5 Hz)
- ***Stage 4:*** Sleep is deepest (delta waves with least frequency (0.5-1.5 Hz)

✓ **Characteristics:**

1- No rapid eye movements.
2- Sleep talking and walking.
3- No dreams (dreams are not consolidated in memory so cannot be remembered).
4- Decreased pulse, blood pressure respiration and basal metabolic rate.

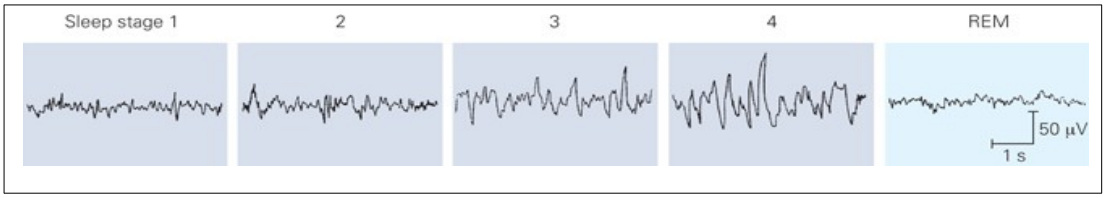
2- Rapid Eye Movement (REM, desynchronized or paradoxical) sleep:

- This type is characterized by rapid roving eye movements and it normally f*ollows the 4th stage* of slow wave *sleep.* The EEG shows desynchronized *beta rhythm* as that encountered in the arousal response. This indicates *brain activity,* but the person is still asleep (so this type of *Sleep* is also called *paradoxical sleep).*
- In a normal night of sleep, bouts of REM sleep lasting 5 to 30 minutes usually appear on the average every 90 minutes. It is repeated 4-5 times/ night. It occupies 20% of sleep hours in adults. It is about 50% in infants and it decreases by age, fatigue and increases by rest.

✓ **EEG changes:** rapid irregular low voltage B waves like that in alert state (desynchronized beta rhythm) (18-30 Hz). This type of sleep is also called paradoxical sleep because it indicates marked brain activity but person is still asleep.

✓ **Characteristic:**

1- Rapid eye movement.
2- Dreams that can be remembered.
3- Marked decrease in muscle tone.
4- Irregular or increased pulse, blood pressure and respiration.
5- Deep sleep difficult to be aroused.



EEG during various stages of the

	Slow wave sleep (non-REM)	**Rapid eye movements sleep (REM)**
1- Timing	Most sleep during night (**80%** of the sleeping time) each period lasts about 90 minutes.	Occurs in episodes during night (**20%** of sleep time) each period lasts about 20 minutes.
2- Brain waves	Four stages: EEG becomes slower with high amplitude ***Stage 1:*** very light sleep (theta waves) ***Stage 2:*** light sleep (sleep spindles within theta) ***Stage 3:*** moderately deep sleep (delta waves) ***Stage 4:*** Sleep is deepest (delta waves with maximal slowing)	One stage: EEG record **Beta waves** (similar to waves of alert person so called *paradoxical sleep*) i.e. brain is active in spite of sleep.
3-Eye movements	Eye deviates up and miosis	Rapid eye movement
4- Importance	Physical rest	Mental rest
5- Autonomic changes	10-30 % decrease in heart rate, arterial blood pressure, respiratory rate and basal	May increase (Increased ***sympathetic*** activity).

	metabolic rate (increased ***parasympathetic*** activity).	
6- Sleep talking & walking	Present	Absent
7- Dreams	Dreams occur but are not remembered.	Active remembered dreams.
8- Penile erection	Absent	Present
9- Teeth grinding	Absent	Present
10- Growth hormone	Increase	Decrease
11- Muscle tone	Slightly inhibited	Extremely inhibited
12- Threshold of arousal	**Low** (person is easier to be aroused)	**High** (person is difficult to be aroused, but we get up in the morning during this stage).

- **Distribution of Sleep Stages:**

- In a typical night of sleep, a young adult first enters NREM sleep, passes through stages 1 and 2, and spends 70–100 minutes in stages 3 and 4, and then a REM period follows.

- This cycle is repeated at intervals of about 90 minutes throughout the night. The cycles are similar, though there is ***less stage 3 and 4 sleep and more REM sleep*** toward morning. Thus, four to six REM periods occur per night. REM sleep occupies 20% of total sleep time in adults and 50% in infants.

Source: Barrett KE, Barman SM, Boitano S, Brooks H: *Ganong's Review of Medical Physiology, 23rd Edition*: http://www.accessmedicine.com

Normal sleep cycles: *REM sleep is indicated by the*

- **The sleep-wakefulness cycle:**

- Once wakefulness starts, it continues by the +ve feedback of excitation of the ARAS. However, after wakefulness continues for many hours sleep tends to occur due to:
  (a) Gradual fading away of the +v feedback cycle.
  (b) Spontaneous activation of the sleep centers which inhibit the ARAS.
- Then during the sleeping hours, the ARAS gradually recovers its excitability while the sleep centers become less excitable because of their overactivity, so the ARAS is released from their inhibitory effect and discharges excitatory signals to the cerebral cortex leading to a new period of wakefulness.

Note:

- Most living cells have rhythmic fluctuations in their function on a circadian cycle. Normally they become entrained, that is, synchronized to the day–night light cycle in the environment.
Melatonin released from pineal gland plays a role in sleep mechanisms. The entrainment process in most cases is dependent on the **suprachiasmatic nuclei (SCN)**. These nuclei receive information about the light–dark cycle via a special neural pathway, the **retinohypothalamic fibers.** Efferents from the SCN initiate neural and humoral signals that entrain a wide variety of well-known circadian rhythms including the sleep–wake cycle and the secretion of the pineal hormone melatonin.
- *Melatonin synthesis and secretion are increased during the dark period of the day and maintained at a low level during daylight hours. The diurnal change in melatonin secretion may function as a timing signal to coordinate events with the light–dark cycle in the environment.*
- *Retinohypothalamic fibers synapse in the suprachiasmatic nuclei (SCN), and there are connections from the SCN to sympathetic preganglionic neurons in the spinal cord that project to the superior cervical ganglion. Postganglionic neurons project from this ganglion to the pineal gland that secretes melatonin*. The cyclic activity of SCN sets up a circadian rhythm

for melatonin release. This rhythm is entrained to light/dark cycles by neurons in the retina.

- **Sleep disorders:**

- **Narcolepsy** is a chronic neurological disorder caused by the brain's inability to regulate sleep–wake cycles normally in which there is a sudden loss of voluntary muscle tone i.e **(cataplexy)**, with an eventual irresistible urge to sleep during daytime. Narcolepsy is characterized by a sudden onset of REM sleep, unlike normal sleep which begins with NREM, slow-wave sleep. Brains from humans with narcolepsy often contain fewer **hypocretin (orexin)**-producing neurons in the hypothalamus.

- **Obstructive sleep apnea (OSA)** is the most common cause of daytime sleepiness due to fragmented sleep at night. Breathing ceases for more than 10 s due to reduction in muscle tone. The apnea (caused by obstruction of the upper airway) causes brief arousals from sleep in order to reestablish upper airway tone. Snoring is a common patient complaint.

- **Somnambulism** (sleepwalking), episodes of sleepwalking are more common in children than in adults and occur predominantly in males. They may last several minutes. Somnambulists walk with their eyes open and avoid obstacles, but when awakened they cannot recall the episodes**.**

- **Nocturnal enuresis** (bed wetting)**,** and **night terrors** are referred to as **parasomnias,** which are also common sleep disorders.

- **Insomnia** (difficult to fall asleep or lack of sleep), as in anxiety, too much caffeine & nicotine and endocrinal disorders e.g hyperthyroidism..